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(54) Title: GENE PROFILING ARRAYS

(57) Abstract: Ordered arrays of mixtures of nucleic acid molecules are provided, which mixtures reflect the expression profile of one or more specimens, such as different cells or tissues. In particular embodiments, complete mRNA mixtures from specimens are separately arrayed on a substrate. Specimens from which such mixtures of nucleic acid molecules are produced can be taken from any source, including animal, plant and/or microbial cells, and can be assembled in any collection desired. The collections can, for instance, include different cell types, different phenotypes, cells grown under different conditions, cells of different ages or developmental stages, and so forth. The nucleic acid arrays are provided in both macro- and microarray formats, and are suitable for gene profiling in which relative quantitative expression from a single source or multiple sources may be determined. Techniques are also disclosed for producing high-fidelity, amplified mixtures of nucleic acid molecules using a combination of anti-sense RNA amplification and template-switching synthesis. Amplified mixtures produced using this method can, for instance, be applied to the disclosed arrays. The disclosed arrays allow high throughput analysis of differential gene expression in a specimen (such as a tumor) or a variety of specimens (such as a variety of tumors), and are suitable for automated preparation and analysis.

## INTERNATIONAL SEARCH REPORT

International Application No.

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A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ZHAO N ET AL: "High-density cDNA filter analysis: a novel approach for large-scale, quantitative analysis of gene expression" GENE, ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, NL, vol. 156, no. 2, 1995, pages 207-213, XP004042356 ISSN: 0378-1119 see whole doc.	1-15, 30-42, 44-57, 59-72
Y	---	16-29, 43, 58
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	SCHMIDT W.M. ET AL.,: "Capselect: a high sensitive method for 5' cap-dependent enrichment of full-length cDNA in PCR-mediate analysis of mRNAs" NUCLEIC ACID RESEARCH, vol. 27, no. 12, - 1999 page e31 XP002211678 see whole doc. esp. p.ii, 1col. 1.par and figure 1.	16-29, 43, 58
A	WO 97 24455 A (CLONTECH LAB INC) 10 July 1997 (1997-07-10) see whole doc. esp. figures and claims	
A	DUGGAN D J ET AL: "EXPRESSION PROFILING USING CDNA MICROARRAYS" NATURE GENETICS, NEW YORK, NY, US, vol. 21, no. SUPPL, January 1999 (1999-01), pages 10-14, XP000865980 ISSN: 1061-4036 the whole document	
A	WO 98 55502 A (SMITHKLINE BEECHAM CORP ; BERGSMAN DERK J (US); MOONEY JEFFREY L (US) 10 December 1998 (1998-12-10) the whole document	
A	WO 99 25873 A (INCYTE PHARMA INC) 27 May 1999 (1999-05-27) see whole doc. esp. claims and figures	
P, X	WANG ENA ET AL.,: "high-fidelity mRNA amplification for gene profiling" NATURE BIOTECHNOLOGY, vol. 18, - April 2000 (2000-04) pages 457-459, XP002211679 the whole document	1-72

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/09993

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9724455	A	10-07-1997	US 5962271 A	05-10-1999
			EP 0871780 A2	21-10-1998
			JP 2000502905 T	14-03-2000
			WO 9724455 A2	10-07-1997
			US 5962272 A	05-10-1999
WO 9855502	A	10-12-1998	EP 0988313 A1	29-03-2000
			JP 2002504820 T	12-02-2002
			WO 9855502 A1	10-12-1998
			US 6187544 B1	13-02-2001
WO 9925873	A	27-05-1999	US 5932451 A	03-08-1999
			CA 2311238 A1	27-05-1999
			EP 1032704 A1	06-09-2000
			JP 2001523471 T	27-11-2001
			WO 9925873 A1	27-05-1999